

Depression, Anxiety, and Sucidality in U.S. Medical Students: A Literature Review and Commentary

By

Kate Dickson

A Master's Paper submitted to the faculty of
the University of North Carolina at Chapel Hill
in partial fulfillment of the requirements for
the degree of Master of Public Health in
the Public Health Leadership Program

Chapel Hill

Summer 2018



Sue Tolleson-Rinehart, PhD
Advisor and first reader

26 June 2018

Date



Samantha Meltzer-Brody MD MPH

26 June 2018

Date

Abstract

A growing body of literature shows that although medical students start their journey to becoming a physician with similar self-reported mental health outcomes as those of their non-medical peers, they finish their training in poorer mental health. Research on the topic of medical student mental health and wellbeing has found higher rates of anxiety, depression, and suicidality among medical students than in the general population, although exact estimates vary by study. A high quality systematic review with meta-analysis of the data on the prevalence of these disorders in medical schools nationwide would help the medical education community more fully understand the scope of the problem, and design interventions appropriately. This paper intended to conduct such a review, but limitations in the literature – especially the paucity of data on anxiety and suicidality - make such synthesis and analysis difficult, if not impossible. This paper presents the findings of the literature review, comments on the gaps and limitations of the evidence, and poses recommendations aimed at improving the quality of the research surrounding medical student mental health.

Table of Contents

Abstract.....	ii
Introduction.....	1
Background.....	1
Rationale.....	3
Methods.....	4
Search Strategy.....	4
Study Selection.....	4
Data Extraction.....	5
Results.....	6
Search Results.....	6
Study Results	6
Discussion.....	7
Characteristics and Limitations of the Existing Literature.....	7
Recommendations for Future Research.....	11
Looking Long Term.....	12
Conclusion.....	13
References.....	15
Appendix A: Tables and Figure.....	21
Table 1: Inclusion and Exclusion Criteria.....	21
Figure 1: Diagram of Search Results.....	22
Table 2; Results of the Literature Review.....	23
Table 3: Measures of Depression.....	28
Table 4: Measures of Anxiety.....	28
Table 5: Measures of Suicidality.....	29
Table 6: Studies by Class Year	29
Appendix B: Search Strategy.....	30
Appendix C: Systematic Review.....	31
Figure C1: PRISMA Diagram.....	40
Table C1: Study Characteristics.....	41
Table C2: Quality Assessment of Articles using the Axis Tool.....	43

Introduction

Background

A growing body of literature reports that, although the exact estimates vary by study, rates of mental illness, specifically depression, anxiety, and suicidality, are higher among physicians and physicians-in-training (medical students, residents, and fellows), than among cohorts of age-matched peers not in the medical field. Studies show that while medical students enter school with similar or better self-reported mental health than is true of others their age, their mental health by the time they graduate is poorer.¹ Furthermore, the mental health of medical students actually declines as they advance in training, both throughout medical school and into residency.¹ Numerous variables contribute to the poor mental health of doctors and those who will become doctors, including long hours, exposure to stressful and traumatic experiences, a culture of perfection, and a strict, hierarchical work environment.^{1,2,48} These, and many other causes, combine to paint a picture of mental illness within the medical community that has severe and far-reaching consequences, for both individuals and for the entire health care system.

In 2015, a study in the Journal of the American Medical Association (JAMA), reported that around 300-400 physicians in the United States commit suicide each year, the equivalent of about 2 graduating medical school classes.² Another study found that rates of suicide are 70% higher among male physicians and 130% higher among female physicians than among non-physicians of the same age and sex.³ Unfortunately, this alarming trend starts early on, in medical school, where suicide is the second leading cause of death among medical students behind accidents, and suicidal ideation is more

common than among non-medical peers of the same age.⁴ If we consider suicide as the most extreme consequence of poor mental health, and medical school as the beginning of a long, arduous journey to becoming a physician, then it is obvious that we need to understand what increases a medical student's risk of committing suicide.

Anxiety and depression are two of the most common mental illnesses in the general population, so it is no surprise that they also occur frequently among medical students. The relationship between depression, anxiety, and suicidality, which includes suicidal ideation, prior suicide attempts, and completed suicides, is well documented. Depression and anxiety, both independently, and often comorbidly, significantly worsen a person's quality of life and are known risk factors for suicide.^{3,5-7} Both are also often manageable conditions, if identified and treated appropriately with psychotherapy and/or medication. Thus, among many necessary steps toward improvement, it is important to understand just how many medical students are suffering from these diseases so that we can attempt to prevent the most severe outcome of their distress – a suicide.

In addition to lowering quality of life and increasing suicidality, poor mental health in providers is associated with worse care for patients. Provider anxiety, depression, and burnout are shown to increase cynicism, worsen communication, and lead to more medical errors.⁸ Specifically, a study of residents published in 2002 found that, when they were asked to reflect on aspects of their own practice, residents with poor mental health were 2 to 3 times more likely to report providing suboptimal patient care.⁹ These data show that the wellbeing of providers is a public health concern. In order to have healthy communities, we need healthy physicians, and healthy physicians learn the habits that promote their mental health and wellbeing early on in medical school. In

fact, acknowledging this relationship has impelled the medical community to add a fourth aim of improving provider mental health and career satisfaction to the Triple Aim of improved patient experience of care, improved population health, and reduced cost.⁵⁷⁻⁵⁸ In recent years, several academic hospital systems, residency programs, and medical schools have formally adopted the “Quadruple Aim” as a way to formalize their commitment to improving the wellness of physicians and physicians-in-training.^{59,60} It is clear that an understanding of the mental health and wellbeing of medical students is critical for the development of a healthy workforce of physicians, and of healthy communities more broadly.

Rationale

This paper originally set out to conduct a systematic review and meta-analysis of the prevalence of depression, anxiety, and suicidality among allopathic medical students in the United States. Much of the existing literature focuses on residents, fellows, and attending physicians, as well as international medical students. However, because American medical education is such a unique experience - 4 dedicated years of study after an undergraduate degree - a synthesis of the data focusing solely on that population is needed.

However, early on in the search process, it became evident that we must address large gaps in the literature before a high quality systematic review leading to meaningful conclusions can be conducted. For that reason, this paper is a review of the state of the literature and a commentary on the gaps and limitations that my search identified. It is accompanied by a discussion of how better data can be collected and why it is necessary to do so, if the medical education community is to truly address the

issue of poor mental health in medical students.

Methods

Search Strategy

I searched PubMed, PsychInfo, and Embase for studies of U.S. medical student mental health and wellbeing published in English between January 1, 2012 and April 17, 2018. Searches included terms related to both medical students and medical school, and the outcomes of interest: depression, anxiety, and suicidality. In PubMed, Medical Subject Headings (MeSH terms) were used as search terms when available. The full search strategy is presented in Appendix B below. I also searched ClinicalTrials.Gov for unpublished literature on the topic, and I searched Prospero for ongoing systematic reviews on the topic, but neither produced relevant results. In addition, although other systematic reviews were excluded from this investigation, the bibliographies of relevant studies were examined to complete the article search process.

Study Selection

I reviewed titles, abstracts, and full-text articles to determine eligibility using the pre-defined inclusion and exclusion criteria. Full inclusion and exclusion criteria are presented in Table 1. Only studies involving students at allopathic medical schools in the United States were included. Eligible studies measured student anxiety, depression, or suicidality using a variety of measures, which are reported in the results of this paper.

This literature review specifically did not include studies that only addressed burnout syndrome, defined as a triad of emotional exhaustion, depersonalization, and a low sense of personal accomplishment. Burnout has recently received a lot of attention

in the medical community because it, too, is a risk factor for suicidality and other poor outcomes for both patients and providers.^{3,13} However, I decided to exclude studies that measured either burnout alone, or without one of the other measures of interest, anxiety, depression, or suicidality, in order to focus more on the universal forms of mental illness likely to affect students at the beginning of their training. Additionally, anxiety and depression are both risk factors for developing burnout, so if the medical community only focuses on the outcome of burnout, it will miss two significant underlying mental health problems that put students at an increased risk.^{8,11,12}

The year 2012 was chosen as the start point for the review because it was the year that the American Medical Association (AMA) published “Supporting Two-Interval Grading Systems for Medical Education”, a policy publicly acknowledging the benefits of a pass-fail curriculum on medical student wellbeing, and encouraging medical schools to adopt such grading systems.¹⁰ To date, a pass-fail grading policy remains one of the few documented interventions that has consistently proven to benefit student mental health and wellbeing. By 2013, 41% of US allopathic schools had adopted pass-fail grading in the pre-clinical curriculum, making it the most common grading method nationwide.¹⁰ Because this major shift in medical education in favor of student mental health occurred in 2012, my review focuses on studies that have been published since then.

Data Extraction

A preliminary data extraction was completed for the studies that met the search criteria outlined in Table 1. The data I extracted included the year of training of the study participants, the specific tools used to measure anxiety, depression, and

suicidality, and also any other wellness-related outcome measures used in the studies.

Results

Search Results

A total of 39 studies were identified in the literature review. The identified studies measured anxiety, depression, suicidality, or some combination of those outcomes of interest among U.S. allopathic medical students. Figure 1 presents the full results of the literature search, and Table 2 includes all 39 articles.

Study Results

As shown in Figure 1, of the 39 studies identified, 38 measured depression, but only 16 also measured anxiety, and only 8 assessed suicidality. Of the 16 studies that measured both anxiety and depression, 4 used a single, combined assessment tool, either the Patient Health Questionnaire-4 item screen (PHQ-4), the Hospital Anxiety and Depression Survey (HADS), or the Depression, Anxiety, and Stress Scale (DASS-21). One study measured suicidality alone without measuring either depression or anxiety. Only 3 studies measured all 3 outcomes of interest. Of note, 5 of the studies identified as measuring both anxiety and depression came from the same set of original data. The Medical Student Cognitive Habits and Growth Evaluation Study (CHANGES) was a multi-center longitudinal survey of first year students at 50 U.S. medical schools. It collected data on over 4,000 medical students nationwide, and several studies on student mental health and wellbeing in recent years have published using the data.

The specific tools used to measure the 3 outcomes of interest varied widely. For depression, the tools included the Patient Health Questionnaire (PHQ) 2-item and 9-item screens, the Patient Reported Outcomes Measurement Information System

(PROMIS) – Emotional Distress and Depression Short Form, the Center for Epidemiological Studies Depression Scale (CES-D), the Beck Depression Inventory, the Harvard National Depression Screen, and the General Depression Scale. To measure anxiety, the PROMIS – Anxiety Short Form, the Spielberger State Anxiety Inventory (SSAI), the Generalized Anxiety Disorder (GAD) – 7, and the Beck Anxiety Inventory were used. As mentioned previously, one study used the PHQ-4, one used the HADS and 2 studies used the DASS-21 to measure both anxiety and depression with the same tool. To assess suicidality, one study used the Meehan Suicide inventory, while the others used various questionnaires ranging in length from 1 to 5 items. Of note, the 4 studies that used a 5-item risk assessment used data from the same original data set, collected by the Healer Education Assessment and Referral (HEAR) Program at UC-San Diego.

A minority of studies only asked participants to report the presence of anxiety or depression rather than using validated survey tools. Tables 3-5 present the full range of measurement tools used by the identified studies to measure the three outcomes of interest.

The 39 studies identified also included students in a variety of class years. The majority of studies included either only first year students (N=10), or students in all 4 years of the traditional U.S. curriculum (N=16). A full breakdown of the studies by student year of participants is presented in Table 6.

Discussion

Characteristics and Limitations of the Existing Literature

One clear characteristic of the literature to date on the topic of depression,

anxiety, and suicidality in U.S. medical students is the heterogeneity of the tools researchers have used to measure these outcomes. For depression, the most frequently measured outcome, 12 different tools were used among 38 studies. Since no single, universal tool for measuring depression has been established, this is common for literature on the topic. As long as the instrument chosen by researchers in each study is valid, the data from multiple studies can be analyzed together by dichotomizing each of the tools into categories of “depressed” or “not depressed” based on the published cut-off values for each tool. The only challenge then is that the person conducting the analysis must be sure that each of the different tools has been validated, and that all studies interpreted their data according to the published guidelines.

Most mental health research is limited by the fact that the majority of instruments used to screen for and diagnose mental illness are self-reported, and this particular body of literature is no different. All of the studies included in this review used voluntary completion of self-reported surveys to measure outcomes, which makes them susceptible to both selection bias and measurement bias. Especially when the topic is sensitive and stigmatized, like mental illness, people might choose not to participate and those that do participate might not be honest with their responses. This limitation is largely unavoidable, but should be kept in mind when analyzing the data that exists on medical student mental health and wellbeing.

Another striking limitation of the literature identified by my review is that, although all but one of the studies measured depression (N=38), studies that measured anxiety and suicidality were much more limited. Specifically, only half of the studies measured anxiety (N=16), and less than one quarter measured suicidality (N=8). This is

problematic because of how tightly interrelated these three forms of mental illness are. For example, high rates of comorbidity between anxiety and depression have been well established.^{8,15} The 2005 U.S. National Comorbidity Survey found that 58% of people with major depression have a comorbid anxiety disorder, and 67% of people with generalized anxiety have a history of unipolar depression. Furthermore, the survey found that those with major depression and comorbid anxiety have poorer outcomes than do those with only one disorder, including more severe disease and a longer, more chronic course.¹⁵ In addition to more severe depression, students with poorly managed anxiety are also at higher risk for other adverse outcomes such as higher perceived stress, lower self-reported quality of life, and higher rates of burnout.^{11,15} A paper written in 1998 about burnout in the medical profession postulated that people who are more sensitive to anxiety are at higher risk of experiencing the exhaustion and depersonalization characteristic of burnout.¹¹ Clearly, if the medical education community is going to attempt to measure and address high rates of depression and burnout in its students, similar attention should be devoted to measuring anxiety.¹¹

The data on suicide returned by the literature review were even more limited. Although rates of suicide are known to be higher in the medical profession than in the general population, the vast majority of articles did not address suicide at all. Among the 8 articles that did measure suicidal ideation or past suicide attempts, the assessment tools varied widely in their scope and validity. Some only asked a single, self-reported screening question, while others, all from the HEAR program at UC- San Diego, included a more thorough 5-item risk assessment. Such infrequent and heterogeneous outcome measures limit the ability of researchers to conduct high quality

data synthesis and analysis on the prevalence of suicidality among medical students. Of course, one reason that the data collected on this topic is so sparse is because of the ethical issues that arise from assessing risk of suicide. Positive responses warrant intervention, so schools that are committed to asking their students about suicidality have a responsibility to follow up with students who endorse it.

As mentioned before, anxiety and depression are both major risk factors for suicide.^{3,5} In fact, anxiety, which was not measured frequently or consistently in the articles identified, acts both independently as a risk factor for suicide (OR 2.29 for ideation and 2.48 for attempts) and amplifies the increased risk of suicide associated with a diagnosis of depression.⁵ As shown by this review, the majority of the research in medical education right now only focuses on depression, while the assessment of anxiety and suicidality is currently inadequate. However, because of the well-established relationship between these 3 outcomes, I would argue that it is unethical for the medical community to ask about symptoms of depression in students without including validated screening tools for both anxiety and the risk of suicide.

The final limitation I identified in the literature review was the wide heterogeneity of study subjects and a lack of follow-up throughout medical school. The traditional medical school curriculum in the United States is 4 years, and the literature varies significantly as to which years of study are included in individual articles. The vast majority of articles surveyed either only first year students (N=10) or students in all 4 years of study (N=16), but the remaining looked at students in some combination of other years. Most articles also were cross-sectional in design, only including data from students at one point in time. Since the learning environment and the stressors of each

year of study differ- for example second year students are traditionally studying hard for the USMLE Step 1 exam, while third year students are experiencing a transition to clinical rotations- it is important to follow students along their entire trajectory of medical education. The current state of the data is characterized by a lack of longitudinal data and a lack of data on students in their last 3 years of schooling in general, since many studies limit themselves to first-year students.

Recommendations for Future Research

After reviewing the literature on the topic of anxiety, depression, and suicidality in U.S. medical students, it is my strong recommendation that the field of medical education use well-validated assessment tools in order to consistently and frequently measure rates of mental illness among students. While several screening tools for anxiety, depression, and suicidality exist, the exact tools that schools choose to use are less important than choosing a reliable and valid instrument, and interpreting it correctly. Schools should assess students each year in order to gain a more longitudinal picture of mental health throughout their medical school trajectory.

Of course, with increased measurement of the prevalence of mental illness among medical students comes an increased responsibility on the part of medical schools to address the needs that arise. Along with screening students more frequently, schools need to invest in their capacity to follow up with students who endorse mental illness and provide evidence-based interventions. Although most assessments will be anonymous, students should be given the opportunity to provide their contact information if they want to receive resources, and schools should work to establish a stigma-free environment where students feel safe reporting honest answers

and asking for help when needed.

Looking Long Term

I believe the gaps and limitations identified in the body of literature surrounding medical student mental health highlight a fundamental misalignment within the field of medical education. Specifically, a disconnect exists between what problems many medical schools' wellness initiatives and programs are designed to solve, and the problems a high number of students actually face. In the words of one student participating in a focus group I conducted on medical student mental health and wellbeing, "I feel like the wellness program that my school has in place is designed to support my wellness more broadly, but not my specific mental health needs."

In other words, the term *wellness* as it applies to medical students encompasses several important domains including physical health, mental health, social health (and healthy relationships), and academic success. In my own experience and the experience of several students in my focus groups, school wellness programs often serve a mostly social role, primarily by organizing fun events for students as study breaks, and secondarily by promoting healthy coping skills such as yoga or mindfulness. What is often missing is recognition of the more difficult aspects of wellness, such as helping students to be successful as they manage underlying mental health diagnoses of anxiety and depression. To give two examples, one student in a focus group mentioned not qualifying for extra academic support when she felt her anxiety was interfering in her test performance because she wasn't doing "poorly enough", and another spoke about not receiving assistance from the school when trying to maintain a standing appointment with a psychiatrist during third year clinical rotations.

These instances show that a lot of students are “left out” of the wellness programs at their schools because it is difficult, if not impossible, to engage with school-sponsored “wellness” events when more basic, underlying mental health needs are not being met.

This literature review shows that clinical mental health issues such as anxiety, depression, and suicidality are under-addressed in the existing literature on medical student wellness, which might partially explain why they are also so under-addressed in medical school programming. My final recommendation is that the medical education community increase the collection of high- quality data about mental health issues among medical students, and use those data to design interventions that meet all students’ mental health needs - from fostering social and physical wellness by organizing friendly team-based competitions, to supporting students’ clinical diagnoses of depression and anxiety by affording them time during rotations specifically for personal appointments.

Conclusion

Although rates of anxiety, depression, and suicidality are known to be higher among medical students than among age-matched peers outside of medicine, the body of literature that measures the prevalence of these outcomes has many gaps and limitations. First, like most mental health research, studies use a wide array of different self-reported tools to measure outcomes. As long as all instruments are validated the heterogeneity is acceptable, but researchers should be aware of the selection bias and measurement bias that arise from voluntary completion of self-reported survey tools. Second, there is much more attention afforded to measuring depression among medical students than there is to measuring either anxiety or suicidality. As shown above, all 3

of these outcomes are not only related, but anxiety and depression are both major risk factors for suicide - the most extreme outcome of poor mental health. If the medical education community is to address the wellbeing of students, then the prevalence of these diseases should be measured consistently and longitudinally. With better data, the medical education community can better design interventions aimed at improving not only the broader wellness of U.S. medical students, but also their basic mental health outcomes. Ensuring that the next generation of physicians is healthy is critical to ensuring that our communities are healthy as well.

References

1. Brazeau, C. M. L. R., Shanafelt, T., Durning, S. J., Massie, F. S., Eacker, A., Moutier, C., ... Dyrbye, L. N. (2014). Distress among matriculating medical students relative to the general population. *Academic Medicine : Journal of the Association of American Medical Colleges*, 89(11), 1520–1525. <https://doi.org/10.1097/ACM.0000000000000482>
2. Goldman, M. L., Shah, R. N., Bernstein, C. A., Khan, R., Lin, J. S., & Mata, D. A. (2015, August). Addressing Depression and Suicide Among Physician Trainees. *JAMA Psychiatry*. United States. <https://doi.org/10.1001/jamapsychiatry.2015.0639>
3. Dyrbye, L. N., Thomas, M. R., Massie, F. S., Power, D. V., Eacker, A., Harper, W., ... Shanafelt, T. D. (2008). Burnout and suicidal ideation among U.S. medical students. *Annals of Internal Medicine*. <https://doi.org/10.7326/0003-4819-149-5-200809020-00008>
4. Grossman, D. C. (2016). Reducing the Stigma: Faculty Speak Out About Suicide Rates Among Medical Students, Physicians. Retrieved June 3, 2018, from <https://news.aamc.org/medical-education/article/reducing-stigma-suicide-rates/>
5. Sareen, J., Cox, B. J., Afifi, T. O., de Graaf, R., Asmundson, G. J., ten Have, M., & Stein, M. B. (2005). Anxiety disorders and risk for suicidal ideation and suicide attempts. *Archives of General Psychiatry*, 62(11), 1249–1257. <https://doi.org/10.1001/archpsyc.62.11.1249>
6. Paro, H. B. M. S., Morales, N. M. O., Silva, C. H. M., Rezende, C. H. A., Pinto, R. M. C., Morales, R. R., ... Prado, M. M. (2010). Health-related quality of life of medical students. *Medical Education*, 44(3), 227–235. <https://doi.org/10.1111/j.1365-2923.2009.03587.x>
7. Brenes, G. A. T. (2007). Anxiety, Depression, and Quality of Life in Primary Care Patients. *Anxiety J Clin Psychiatry Prim Care Companion J Clin Psychiatry*, 99(6), 437–443. Retrieved from <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2139931/pdf/i1523-5998-9-6-437.pdf>
8. Silva, V., Costa, P., Pereira, I., Faria, R., Salgueira, A. P., Costa, M. J., ... Morgado, P. (2017). Depression in medical students: insights from a longitudinal study. *BMC Medical Education*, 17. <https://doi.org/10.1186/s12909-017-1006-0>
9. Shanafelt T Bradley K Wipf J Back A. (2002). Burnout and Self-Reported Patient Care in an Internal Medicine Residency Program. *Annals of Internal Medicine*, 136 (5)(February 2001), 358. <https://doi.org/200203050-00008> [pii]
10. Deng, F. and Wesevich, A. (2016). Pass-fail is here to stay in medical schools. And that's a good thing. *KevinMD.com*. <https://www.kevinmd.com/blog/2016/08/pass-fail-stay-medical-schools-thats-good-thing.html>
11. Turnipseed, D. L. (1998). Anxiety and Burnout in the Health Care Work Environment. *Psychological Reports*, 82, 627–642. Retrieved from <http://journals.sagepub.com.libproxy.lib.unc.edu/doi/pdf/10.2466/pr0.1998.82.2.627>

12. Monrouxe, L. V, Bullock, A., Tseng, H.-M., & Wells, S. E. (2017). Association of professional identity, gender, team understanding, anxiety and workplace learning alignment with burnout in junior doctors: a longitudinal cohort study. *BMJ Open*, 7(12), e017942. <https://doi.org/10.1136/bmjopen-2017-017942>
13. Shanafelt, T. D., Boone, S., Tan, L., Dyrbye, L. N., Sotile, W., Satele, D., ... Oreskovich, M. R. (2012). Burnout and satisfaction with work-life balance among US physicians relative to the general US population. *Archives of Internal Medicine*, 172(18), 1377–1385. <https://doi.org/10.1001/archinternmed.2012.3199>
14. Hardeman, R. R., Perry, S. P., Phelan, S. M., Przedworski, J. M., Burgess, D. J., & van Ryn, M. (2016). Racial Identity and Mental Well-Being: The Experience of African American Medical Students, A Report from the Medical Student CHANGE Study. *Journal of Racial and Ethnic Health Disparities*. <https://doi.org/10.1007/s40615-015-0136-5>
15. Pollack, M. H. (2005). Comorbid Anxiety and Depression. *J Clin Psychiatry*, 66. Retrieved from http://www.psychiatrist-com.libproxy.lib.unc.edu/JCP/article/_layouts/ppp.psych.controls/BinaryViewer.aspx?Article=/JCP/article/Pages/2005/v66s08/v66s0804.aspx&Type=Article
16. Chang, E., Eddins-Folensbee, F., & Coverdale, J. (2012). Survey of the prevalence of burnout, stress, depression, and the use of supports by medical students at one school. *Academic Psychiatry*. <https://doi.org/10.1176/appi.ap.11040079>
17. Dyrbye, L. N., Eacker, A. M., Harper, W., Power, D. V., Massie, F. S., Satele, D., ... Shanafelt, T. D. (2012). Distress and empathy do not drive changes in specialty preference among US medical students. *Medical Teacher*. <https://doi.org/10.3109/0142159X.2012.644830>
18. Chang, E., Eddins-Folensbee, F., Porter, B., & Coverdale, J. (2013). Utilization of counseling services at one medical school. *Southern Medical Journal*. <https://doi.org/10.1097/SMJ.0b013e3182a05994>
19. Trostler, M., Li, Y., & Plankey, M. W. (2014). Prevalence of binge drinking and associated co-factors among medical students in a US Jesuit University. *American Journal of Drug and Alcohol Abuse*. <https://doi.org/10.3109/00952990.2014.907302>
20. Johnson, K., Simon, N., Wicks, M., Schaad, D., Barr, K. P., & O'Connor, K. (2014). Sleep habits, quality of life and satisfaction with academic success in second year medical students. *Journal of General Internal Medicine*.
21. Wimsatt, L. A., Schwenk, T. L., & Sen, A. (2015). Predictors of Depression Stigma in Medical Students: Potential Targets for Prevention and Education. *American Journal of Preventive Medicine*. <https://doi.org/10.1016/j.amepre.2015.03.021>
22. Liu, R., Carrese, J., Colbert-Getz, J., Geller, G., & Shochet, R. (2015). “Am i cut out for this?” Understanding the experience of doubt among first-year medical students. *Medical Teacher*. <https://doi.org/10.3109/0142159X.2014.9709872015>
23. Tucker, P., Jeon-Slaughter, H., Sener, U., Arvidson, M., & Khalafian, A. (2015). Do Medical Student Stress, Health, or Quality of Life Foretell Step 1 Scores? A Comparison of Students in Traditional and Revised Preclinical Curricula.

Teaching and Learning in Medicine.

<https://doi.org/10.1080/10401334.2014.979178>

24. Ludwig, A. B., Burton, W., Weingarten, J., Milan, F., Myers, D. C., & Kligler, B. (2015). Depression and stress amongst undergraduate medical students. *BMC Medical Education*. <https://doi.org/10.1186/s12909-015-0425-z>
25. Brannick, M. T., Horn, G. T., Schnaus, M. J., Wahi, M. M., & Goldin, S. B. (2015). Medical student quality-of-life in the clerkships: A scale validation study. *American Surgeon*.
26. Gold, J. A., Johnson, B., Leydon, G., Rohrbaugh, R. M., & Wilkins, K. M. (2015). Mental health self-care in medical students: A comprehensive look at help-seeking. *Academic Psychiatry*. <https://doi.org/10.1007/s40596-014-0202-z>
27. Thompson, G., McBride, R. B., Hosford, C. C., & Halaas, G. (2016). Resilience Among Medical Students: The Role of Coping Style and Social Support. *Teaching and Learning in Medicine*. <https://doi.org/10.1080/10401334.2016.1146611>
28. Chen, A. K., Kumar, A., & Haramati, A. (2016). The effect of Mind Body Medicine course on medical student empathy: A pilot study. *Medical Education Online*. <https://doi.org/10.3402/meo.v21.31196>
29. Kroska, E. B., Calarge, C., O'Hara, M. W., Deumic, E., & Dindo, L. (2017). Burnout and depression in medical students: Relations with avoidance and disengagement. *Journal of Contextual Behavioral Science*. <https://doi.org/10.1016/j.jcbs.2017.08.003>
30. Wolf, M. R., & Rosenstock, J. B. (2017). Inadequate Sleep and Exercise Associated with Burnout and Depression among Medical Students. *Academic Psychiatry*. <https://doi.org/10.1007/s40596-016-0526-y>
31. Elkins, C., Plante, K. P., Germain, L. J., & Morley, C. P. (2017). Burnout and depression in MS1 and MS3 years: A comparison of cohorts at one medical school. *Family Medicine*.
32. Johnson, K. M., Simon, N., Wicks, M., Barr, K., O'Connor, K., & Schaad, D. (2017). Amount of Sleep, Daytime Sleepiness, Hazardous Driving, and Quality of Life of Second Year Medical Students. *Academic Psychiatry*. <https://doi.org/10.1007/s40596-017-0668-6>
33. Haight S.J.; Chibnall J.T.; Schindler D.L.; Slavin S.J. (2012) Associations of medical student personality and health/wellness characteristics with their medical school performance across the curriculum. *Academic medicine : journal of the Association of American Medical Colleges*
34. McGrady, A., Brennan, J., Lynch, D., & Whearty, K. (2012). A wellness program for first year medical students. *Applied Psychophysiology Biofeedback*. <https://doi.org/10.1007/s10484-012-9198-x>
35. Wachholtz, A., & Rogoff, M. (2013). The relationship between spirituality and burnout among medical students. *Journal of Contemporary Medical Education*. <https://doi.org/10.5455/jcme.20130104060612>
36. Slavin, S. J., Schindler, D. L., & Chibnall, J. T. (2014). Medical Student Mental Health 3.0. *Academic Medicine*. <https://doi.org/10.1097/ACM.0000000000000166>
37. Hardeman, R. R., Przedworski, J. M., Burke, S. E., Burgess, D. J., Phelan, S. M., Dovidio, J. F., ... van Ryn, M. (2015). Mental Well-Being in First Year Medical

- Students: A Comparison by Race and Gender: A Report from the Medical Student CHANGE Study. *Journal of Racial and Ethnic Health Disparities*. <https://doi.org/10.1007/s40615-015-0087-x>
38. Przedworski, J. M., Dovidio, J. F., Hardeman, R. R., Phelan, S. M., Burke, S. E., Ruben, M. a, ... van Ryn, M. (2015). A Comparison of the Mental Health and Well-Being of Sexual Minority and Heterosexual First-Year Medical Students: A Report From the Medical Student CHANGE Study. *Academic Medicine : Journal of the Association of American Medical Colleges*. <https://doi.org/10.1097/ACM.0000000000000658>
 39. Phelan, S. M., Burgess, D. J., Puhl, R., Dyrbye, L. N., Dovidio, J. F., Yeazel, M., ... van Ryn, M. (2015). The Adverse Effect of Weight Stigma on the Well-Being of Medical Students with Overweight or Obesity: Findings from a National Survey. *Journal of General Internal Medicine*. <https://doi.org/10.1007/s11606-015-3266-x>
 40. Hardeman, R. R., Przedworski, J. M., Burke, S., Burgess, D. J., Perry, S., Phelan, S., ... van Ryn, M. (2016). Association Between Perceived Medical School Diversity Climate and Change in Depressive Symptoms Among Medical Students: A Report from the Medical Student CHANGE Study. *Journal of the National Medical Association*. <https://doi.org/10.1016/j.jnma.2016.08.005>
 41. Hardeman, R. R., Perry, S. P., Phelan, S. M., Przedworski, J. M., Burgess, D. J., & van Ryn, M. (2016). Racial Identity and Mental Well-Being: The Experience of African American Medical Students, A Report from the Medical Student CHANGE Study. *Journal of Racial and Ethnic Health Disparities*. <https://doi.org/10.1007/s40615-015-0136-5>
 42. Mousa, O. Y., Dhamoon, M. S., Lander, S., & Dhamoon, A. S. (2016). The MD Blues: Under-Recognized Depression and Anxiety in Medical Trainees. *PLoS ONE*. <https://doi.org/10.1371/journal.pone.0156554>
 43. Damiano, R. F., DiLalla, L. F., Lucchetti, G., & Dorsey, J. K. (2017). Empathy in Medical Students Is Moderated by Openness to Spirituality. *Teaching and Learning in Medicine*. <https://doi.org/10.1080/10401334.2016.1241714>
 44. Chand, S. P., Chibnall, J. T., & Slavin, S. J. (2018). Cognitive Behavioral Therapy for Maladaptive Perfectionism in Medical Students: A Preliminary Investigation. *Academic Psychiatry*. <https://doi.org/10.1007/s40596-017-0708-2>
 45. Lucchetti, G., Damiano, R. F., DiLalla, L. F., Lucchetti, A. L. G., Moutinho, I. L. D., da Silva Ezequiel, O., & Kevin Dorsey, J. (2018). Cross-cultural Differences in Mental Health, Quality of Life, Empathy, and Burnout between US and Brazilian Medical Students. *Academic Psychiatry : The Journal of the American Association of Directors of Psychiatric Residency Training and the Association for Academic Psychiatry*. <https://doi.org/10.1007/s40596-017-0777-2>
 46. Downs, N., Feng, W., Kirby, B., McGuire, T., Moutier, C., Norcross, W., ... Zisook, S. (2014). Listening to depression and suicide risk in medical students: The Healer Education Assessment and Referral (HEAR) program. *Academic Psychiatry*. <https://doi.org/10.1007/s40596-014-0115-x>
 47. Dyrbye, L. N., West, C. P., Satele, D., Boone, S., Tan, L., Sloan, J., & Shanafelt, T. D. (2014). Burnout among u.s. medical students, residents, and early career

- physicians relative to the general u.s. population. *Academic Medicine*.
<https://doi.org/10.1097/ACM.000000000000134>
48. MacLean, L., Booza, J., & Balon, R. (2016). The Impact of Medical School on Student Mental Health. *Academic Psychiatry*. <https://doi.org/10.1007/s40596-015-0301-5>
 49. Jackson, E. R., Shanafelt, T. D., Hasan, O., Satele, D. V., & Dyrbye, L. N. (2016). Burnout and alcohol abuse/dependence among U.S. Medical Students. *Academic Medicine*. <https://doi.org/10.1097/ACM.0000000000001138>
 50. Martinez, S., Tal, I., Norcross, W., Newton, I. G., Downs, N., Seay, K., ... Zisook, S. (2016). Alcohol use in an academic medical school environment: A UC San Diego Healer Education Assessment and Referral (HEAR) Report. *Annals of Clinical Psychiatry: Official Journal of the American Academy of Clinical Psychiatrists*.
 51. Merlo, L. J., Curran, J. S., & Watson, R. (2017). Gender differences in substance use and psychiatric distress among medical students: A comprehensive statewide evaluation. *Substance Abuse*.
<https://doi.org/10.1080/08897077.2017.1355871>
 52. Moutier, C., Norcross, W., Jong, P., Norman, M., Kirby, B., McGuire, T., & Zisook, S. (2012). The suicide prevention and depression awareness program at the university of California, San Diego school of medicine. *Academic Medicine*.
<https://doi.org/10.1097/ACM.0b013e31824451ad>
 53. Zisook, S., Young, I., Doran, N., Downs, N., Hadley, A., Kirby, B., ... Tiamson-Kassab, M. (2016). Suicidal Ideation among Students and Physicians at a U.S. Medical School: A Healer Education, Assessment and Referral (HEAR) Program Report. *Omega (United States)*. <https://doi.org/10.1177/0030222815598045>
 54. Heron M. Deaths: Leading causes for 2015. National Vital Statistics Reports; vol 66 no 5. Hyattsville, MD: National Center for Health Statistics. 2017.
 55. Rotenstein, L. S., Ramos, M. A., Torre, M., Segal, J. B., Peluso, M. J., Guille, C., ... Mata, D. A. (2016). Prevalence of Depression, Depressive Symptoms, and Suicidal Ideation Among Medical Students. *JAMA*.
<https://doi.org/10.1001/jama.2016.17324>
 56. Downes, M. J., Brennan, M. L., Williams, H. C., & Dean, R. S. (2016). Appraisal tool for Cross-Sectional Studies (AXIS). *BMJ Open*. Retrieved from
<http://bmjopen.bmj.com/content/bmjopen/6/12/e011458/DC2/embed/inline-supplementary-material-2.pdf?download=true>
 57. Berwick, D. M., Nolan, T. W., & Whittington, J. (2008). The triple aim: Care, health, and cost. *Health Affairs*, 27(3), 759–769.
<https://doi.org/10.1377/hlthaff.27.3.759>
 58. Bodenheimer, T., & Sinsky, C. (2014). From triple to Quadruple Aim: Care of the patient requires care of the provider. *Annals of Family Medicine*, 12(6), 573–576.
<https://doi.org/10.1370/afm.1713>
 59. Roper, B., & Wesley, B. (2016, August 4). UNC School of Medicine, UNC Health Care officially adopt Quadruple Aim. *UNC School of Medicine Vital Signs*. Retrieved from <http://news.unchealthcare.org/som-vital-signs/2016/aug-4/unc-school-of-medicine-officially-adopts-quadruple-aim>

60. Anandarajah, A. P., Quill, T. E., & Privitera, M. R. (2018). Adopting the Quadruple Aim: The University of Rochester Medical Center Experience: Moving from Physician Burnout to Physician Resilience. *The American Journal of Medicine*. <https://doi.org/https://doi.org/10.1016/j.amjmed.2018.04.034>

Appendix A: Tables and Figures

Table 1: Inclusion and Exclusion Criteria

	Inclusion Criteria	Exclusion Criteria
Population	<ul style="list-style-type: none"> - U.S. Medical students 	<ul style="list-style-type: none"> - Residents - Fellows - Attending Physicians - Foreign medical school students and graduates - Other allied health sciences professionals (nurses, PAs, NPs, physical therapists, veterinarians)
Exposure (Setting)	<ul style="list-style-type: none"> - Allopathic M.D. program at a U.S. Medical School 	<ul style="list-style-type: none"> - Medical schools outside of the U.S. - Other health science degree programs (NP, PA, physical therapy, veterinary, dentistry) - Osteopathic medical schools - Residency or fellowship programs
Comparator group	<ul style="list-style-type: none"> - General population - Other levels of training (residents, fellows, attending physicians) - Other health professionals - No comparator 	N/A
Outcome	<p>One or more of the following:</p> <ul style="list-style-type: none"> - Depression - Anxiety - Suicidality: suicidal ideation, suicide attempts, completed suicides 	<ul style="list-style-type: none"> - Burnout only (without one of the other outcomes of interest) - General wellbeing / wellness scores (without one of the other outcomes of interest)
Time frame	Published 2012-2018	Published before 2012
Study design	<ul style="list-style-type: none"> - Observational studies (cross-sectional or longitudinal, cohort studies) - Randomized or non-randomized trials 	<ul style="list-style-type: none"> - Systematic reviews and meta-analyses - Opinion, commentary, and letters to the editor - Abstracts and oral presentations only

Figure 1. Diagram of Search Results

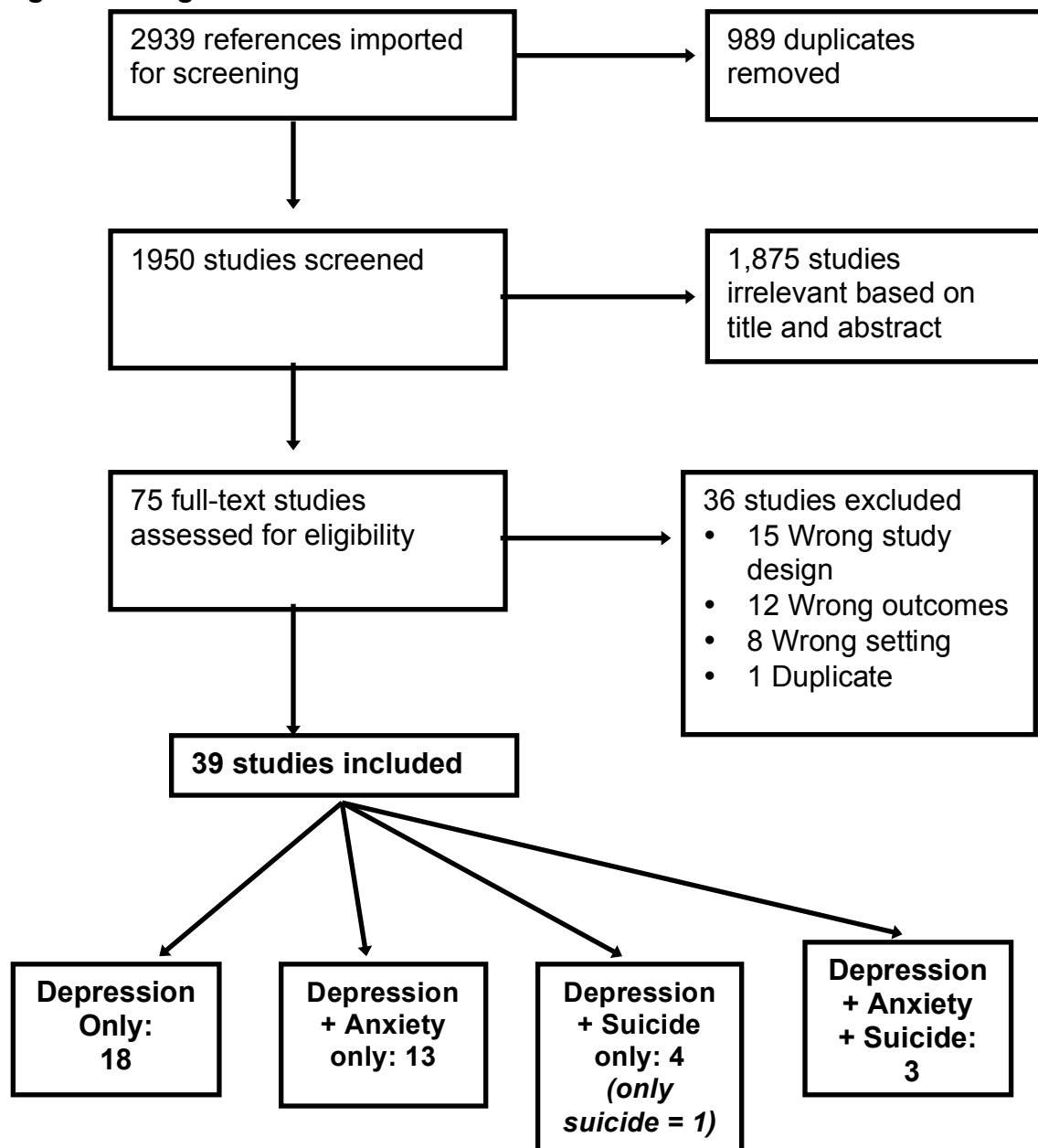


Table 2. Results of Literature Review

Authors	Student Year	Measures				
		Anxiety	Depression	Both	Suicidality	Others
Chang E.; Eddins-Folensbee F.; Coverdale J. (2012) ¹⁶	1, 2, 3		PHQ-2			MBI, Perceived Medical School Stress Scale
Dyrbye LN. Eacker AM.; Harper W.; Power DV.; Massie FS.; Satele D.; Thomas MR.; Sloan JA.; Shanafelt TD. (2012) ¹⁷	1, 2, 3		PHQ-2			MBI, Jefferson Scale of Physician Empathy, MOS QOL SF
Chang E.; Eddins-Folensbee F.; Porter B.; Coverdale J. (2013) ¹⁸	1, 2, 3		modified PHQ-2			MBI
Trostler M.; Li Y.; Plankey MW. (2014) ¹⁹	1, 2, 3, 4		Self Reported			Self reported binge drinking, illicit and non-prescribed prescription drug use, stress level, tobacco use, protective behavioral strategies
Brazeau CM.; Shanafelt T.; Durning SJ.; Massie FS.; Eacker A.; Moutier C.; Satele DV.; Sloan JA.; Dyrbye LN. (2014) ¹	1		PHQ-2			MBI, Linear Analogue Assessment for overall QOL
Johnson K.; Simon N.; Wicks M.; Schaad D.; Barr K.P.; O'Connor K. (2014) ²⁰	2		modified PHQ2			Sleep habits inventory, Epworth sleep scale, one item from MBI, one item from PSS, and one item about emotional wellbeing
Wimsatt LA.; Schwenk TL.; Sen A. (2015) ²¹	1, 2, 3, 4		PHQ-9			Depression Stigma, self reported academic performance, history of depression
Liu R; Carrese J; Colbert-Getz J; Geller G; Shochet R. (2015) ²²	1		Self Reported			9 questions measuring doubt
Tucker P.; Jeon-Slaughter H.; Sener U.; Arvidson M.; Khalafian A. (2015) ²³	1, 2		BDI			PSS, PCS, QOL Satisfaction Questionnaire, adapted Curriculum Stress Questionnaire

Ludwig AB.; Burton W.; Weingarten J.; Milan F.; Myers DC.; Kligler B (2015) ²⁴	1, 3		CES-D			PSS, NHIS sleep habits and substance use scale, Weight, Activity, Variety and Excess tool
Brannick, Michael T, PhD; Horn, Gregory T, MD; Schnaus, Michael J, MD; Wahi, Monika M, MPH, CPH; Goldin, Steven B, MD, PhD, MPH (2015) ²⁵	3		HNDS			MOS Core Measures of QOL 15 item survey, likert scale of fatigue, quantitative sleep hours per night
Gold JA.; Johnson B.; Leydon G.; Rohrbaugh RM.; Wilkins KM. (2015) ²⁶	1, 2, 3, 4		PHQ-2			Single item stress question, modified MBI, Attitudes to Mental Illness Questionnaire, modified AUDIT-C
Thompson G; McBride RB; Hosford CC; Halaas G. (2016) ²⁷	1, 2, 3, 4		PHQ-9			Items pertaining to past diagnosis and treatment of depression, likert scale of social support, coping strategies inventory, MBI
Chen AK.; Kumar A.; Haramati A. (2016) ²⁸	1		PHQ-9			Jefferson Scale of Physician Empathy, PSS
Kroska, Emily B.; Calarge, Chadi; O'Hara, Michael W.; Deumic, Emira; Dindo, Lilian (2017) ²⁹	2, 3, 4		General Depression Scale			MBI, Acceptance and Action Questionnaire-II, Valued Living Questionnaire
Wolf MR.; Rosenstock JB. (2017) ³⁰	1, 2, 3, 4		PHQ-2			Likert scale of subjective wellbeing, MBI, quantitative sleep hours, ESS, Godin Leisure-Time Exercise Questionnaire
Elkins C.; Plante KP.; Germain LJ.; Morley CP (2017) ³¹	1, 3		PHQ-2			MBI
Johnson KM.; Simon N.; Wicks M.; Barr K.; O'Connor K.; Schaad D (2017) ³²	2		modified PHQ2			Sleep habits inventory, ESS, one item from MBI, one item from PSS, and one item about emotional wellbeing
Haight SJ.; Chibnall JT.; Schindler DL.; Slavin SJ. (2012) ³³	3	SSAI	CES-D			NEO Five Factor Personality Inventory, Jefferson Scale of Physician Empathy, PSS, MOS Social Support Inventory, PCS

McGrady A.; Brennan J.; Lynch D.; Whearty K. (2012) ³⁴	1	BAI	BDI			Social Readjustment Rating Scale- Revised, questionnaire about illness frequency
Wachholtz A.; Rogoff M. (2013) ³⁵	1, 2, 3, 4			HADS		Daily Spiritual Experiences Scale, Burnout measure- short version, Functional Assessment of Chronic Illness Therapy- Spiritual Well-Being Non Illness (FACIT-Sp-NI)
Slavin SJ.; Schindler DL.; Chibnall JT. (2014) ³⁶	1, 2	SSAI	CES-D			PSS, PCS, AAMC Graduation Questionnaire, USMLE Step 1 Scores
Hardeman RR.; Przedworski JM.; Burke SE.; Burgess DJ.; Phelan SM.; Dovidio JF.; Nelson D.; Rockwood T.; van Ryn M. (2015) ³⁷	1	PROMIS- Anxiety Short Form	PROMIS- Emotional Distress- Depression Short Form			Self rated health, Brief COPE Inventory, MOS Social Support Survey, Pearlin's Mastery Scale, State Self-Esteem Scale
Przedworski JM.; Dovidio JF.; Hardeman RR.; Phelan SM.; Burke SE.; Ruben MA.; Perry SP.; Burgess DJ.; Nelson DB.; Yeazel MW.; Knudsen JM.; van Ryn M. (2015) ³⁸	1	PROMIS- Anxiety Short Form	PROMIS- Emotional Distress- Depression Short Form			Sexual identity, self rated health, select items from the Everyday Discrimination Scale and the UCLA Loneliness Scale
Phelan SM.; Burgess DJ.; Puhl R.; Dyrbye LN.; Dovidio JF.; Yeazel M.; Ridgeway JL.; Nelson D.; Perry S.; Przedworski JM.; Burke SE.; Hardeman RR.; van Ryn M (2015) ³⁹	1	PROMIS- Anxiety Short Form	PROMIS- Emotional Distress- Depression Short Form			BMI, select items from: State Self-Esteem Scale, Pearlin Mastery Scale, MOS Social Support Survey, UCLA Social Loneliness Scale, Brief COPE measure, Crandall's Anti Fat Attitudes Questionnaire, Fat-Thin IAT, Everyday Discrimination Scale
Hardeman RR.; Przedworski JM.; Burke S.; Burgess DJ.; Perry S.; Phelan S.; Dovidio JF.; van Ryn M. (2016) ⁴⁰	1	PROMIS- Anxiety Short Form	PROMIS- Emotional Distress- Depression Short Form			Perception of institution's racial climate, exposure to negative role models, witnessed discrimination

Hardeman RR.; Perry SP.; Phelan SM.; Przedworski JM.; Burgess DJ.; van Ryn M. (2016) ⁴¹	1	PROMIS-Anxiety Short Form	PROMIS-Emotional Distress-Depression Short Form			Short Form PSS, Multidimensional Inventory for Black Identity
Mousa OY.; Dhamoon MS.; Lander S.; Dhamoon AS. (2016) ⁴²	1, 2, 3, 4	GAD-7	PHQ-2			
Damiano RF.; DiLalla LF.; Lucchetti G.; Dorsey JK (2017) ⁴³	1, 2, 3, 4			DASS-21		ESWIM, 3 general quality of life items, WHO-QOL-BREF, Duke University Religious Index, OLBI
Chand SP.; Chibnall JT.; Slavin SJ. (2018) ⁴⁴	1	SSAI	CES-D			Almost Perfect Scale-Revised, Imposter Scale, Perfectionism sub-scale of the Dysfunctional Attitude Scale
Lucchetti G.; Damiano RF.; DiLalla LF.; Lucchetti ALG.; Moutinho ILD.; da Silva Ezequiel O.; Kevin Dorsey J. (2018) ⁴⁵	1, 2			DASS-21		ESWIM, OLBI, WHO-QOL-BREF
Downs N.; Feng W.; Kirby B.; McGuire T.; Moutier C.; Norcross W.; Norman M.; Young I.; Zisook S. (2014) ⁴⁶	1, 2, 3, 4		PHQ-9		4 item screen	Self reported alcohol and drug use, adapted ASI, current mental health treatment
Dyrbye LN.; West CP.; Satele D.; Boone S.; Tan L.; Sloan J.; Shanafelt TD. (2014) ⁴⁷	1, 2, 3, 4		PHQ-2		Single item screen	MBI, standardized linear scale for overall QOL, standardized linear scale for level of fatigue
Jackson ER.; Shanafelt TD.; Hasan O.; Satele DV.; Dyrbye LN (2016) ⁴⁹	1, 2, 3, 4		PHQ-2		Single item screen	AUDIT-C, MBI, standardized linear scale for overall QOL, standardized linear scale for level of fatigue
Martinez S.; Tal I.; Norcross W.; Newton IG.; Downs N.; Seay K.; McGuire T.; Kirby B.; Chidley B.; Tiamson-Kassab M.; Lee D.; Hadley A.; Doran N.; Jong P.; Lee K.; Moutier C.; Norman M.; Zisook S. (2016) ⁵⁰	1, 2, 3, 4		PHQ-9		4 item screen	Self reported alcohol and drug use, adapted ASI, current mental health treatment

Merlo LJ.; Curran JS.; Watson R. (2017) ⁵¹	1, 2, 3, 4				Self reported	98 item research questionnaire created for this study. Included items on tobacco use, alcohol use, marijuana, prescription drug, opioid, and other illicit drug use, and well being/ distress
Moutier C.; Norcross W.; Jong P.; Norman M.; Kirby B.; McGuire T.; Zisook S. (2012) ⁵²	1, 2, 3, 4	Self reported	PHQ-9		Self reported past suicide attempts	ASI
Zisook, Sidney; Young, Ilanit; Doran, Neal; Downs, Nancy; Hadley, Allison; Kirby, Brittany; McGuire, Tara; Moutier, Christine; Norcross, William; Tiamson-Kassab, Maria (2016) ⁵³	1, 2, 3, 4	Self reported	PHQ-9		4 item screen 3 items from Meehan Suicide Inventory	ASI, global functional impairment, self reported alcohol, substance abuse, and disordered eating 6 questions from Natinal Survey on Drug use and Health, additional questions on perceived health, subjective stress level, and help seeking behavior
MacLean L.; Booza J.; Balon R. (2016) ⁴⁸	1, 2, 3, 4			PHQ4		

PHQ: Patient Health Questionnaire
 MBI: Maslach Burnout Inventory
 MOS: Medical Outcomes Survey
 QOL: Quality of Life
 ESS: Epworth Sleepiness Scale
 PSS: Perceived Stress Scale
 PCS: Perceived Cohesion Scale
 PROMIS: Patient Reported Outcomes Measurement Information System
 CES-D: Center for Epidemiological Studies Depression Scale

HNDS: Harvard National Depression Screen
 HADS: Hospital Anxiety and Depression Scale
 DASS-21: Depression Anxiety and Stress Scale
 SSAI: Spielberger State Anxiety Inventory
 GAD-7: Generalized Anxiety Disorder
 BAI: Beck Anxiety Inventory
 ESWIM: Empathy, Spirituality, and Wellness in Medicine Scale
 OLBI: Oldenburg Burnout Inventory
 AUDIT-C: Alcohol Use Disorders Identification Test
 ASI: Affective States Inventory

Table 3. Measures of Depression

Depression Tool	Number of Studies
Patient Health Questionnaire – 2 item (PHQ-2)	9
Patient Health Questionnaire – 9 item (PHQ-9)	7
Patient Reported Outcomes Measurement Information System (PROMIS)- Emotional Distress/ Depression Short Form	5*
Center for Epidemiological Studies Depression Scale (CES-D)	4
Adapted PHQ-2	3
Beck Depression Inventory (BDI)	2
Harvard National Depression Screen (HNDS)	1
General Depression Scale	1
PHQ- 4 – both depression and anxiety	1
Hospital Anxiety and Depression Scale (HADS) – both depression and anxiety	1
Depression Anxiety and Stress Scale (DASS-21) – both depression and anxiety	2
Other (Self Reported)	2
Total	38

* CHANGES data

Table 4. Measures of Anxiety

Anxiety Tool	Number of Studies
PROMIS – Anxiety Short Form	5*
Spielberger State Anxiety Inventory (SSAI)	3
Generalized Anxiety Disorder (GAD)- 7 item	1
Beck Anxiety Inventory (BAI)	1
PHQ-4 – both anxiety and depression	1
Hospital Anxiety and Depression Scale (HADS) – both anxiety and depression	1
Depression Anxiety and Stress Scale (DASS-21) – both anxiety and depression	2
Other (Self Reported)	2
Total	16

*CHANGES data

Table 5. Measures of Suicidality

Suicidity Tool	Number of Studies
Single item screen	3*
5 item screen	4**
3 items from Meehan Suicide Inventory	1
Total	8

*single questions varied by study

**HEAR Program

Table 6. Studies by Class Year

Class Year Included In Study	Number of Studies
Year 1	10
Year 2	2
Year 3	2
Years 1 and 2	3
Years 1 and 3	2
Years 1, 2, and 3	3
Years 2, 3, and 4	1
Years 1,2,3, and 4	16
Total	39

Appendix B: Search Strategy

Pubmed:

("medical student"[tiab] OR "medical students"[tiab] OR "medical school"[tiab] OR "medical schools"[tiab] OR "medical school student"[tiab] OR "medical school students"[tiab] OR "medical education"[tiab] OR students, medical[mesh]) AND (anxiety OR depress* OR suicide OR suicidal* OR "suicidal ideation" OR anxiety[mesh] OR depression[mesh] OR suicide[mesh] OR ideation, suicidal[mesh])

PsychInfo

AB("medical student" OR "medical students" OR "medical school" OR "medical schools" OR "medical school student" OR "medical school students" OR "medical education") AND (anxiety OR depress* OR suicide OR suicidal* OR "suicidal ideation")

Embase:

('medical student':ab,ti OR 'medical students':ab,ti OR 'medical school':ab,ti OR 'medical schools':ab,ti OR 'medical school student':ab,ti OR 'medical school students':ab,ti OR 'medical education':ab,ti) AND (anxiety OR depress* OR suicide OR suicidal* OR "suicidal ideation")

Appendix C:

Prevalence of Suicidality Among U.S. Medical Students: A Systematic Review

Abstract

Introduction: Rates of suicide are higher among physicians and physicians-in-training than the general population.⁵³ This systematic review focuses on the prevalence of suicidality, defined as suicidal ideation and suicide attempts, among medical students at U.S. medical schools.

Methods: PubMed, PsychInfo, and Embase were searched for studies on the topic published in English between January 1, 2012 and June 2018. ClinicalTrials.Gov and Prospero were also searched for unpublished literature and ongoing systematic reviews. The search strategy included terms related to the population and setting of interest (medical students and medical school), as well as the outcomes of interest for the paper above, including anxiety, depression, and suicidality. For the purposes of this systematic review, only those that measured suicidality were included. Excel was used for data extraction and quality assessment using the AXIS tool.⁵⁶

Results: A total of 8 studies including over 6,000 medical students were identified. Of the 8 studies, 5 were included in the data extraction and quality assessment process.

Prevalence rates of suicidal ideation ranged from 7.9%-11.8%, but the heterogeneity of the studies and the outcome measures used prevented a quantitative meta-analysis.

Conclusions: The body of literature that currently exists on the topic of suicidality in U.S. medical students has many limitations, but it is clear that this is a relatively common problem. In order to address the mental health needs of medical students, high quality research using consistent, well-validated screening tools is necessary.

Introduction

Suicide is the 10th leading cause of death in the United States and a number of highly publicized, celebrity suicides in recent months have increased the general public's awareness of suicide as the most extreme outcome of severe distress and mental illness.⁵⁴ Unfortunately, although suicide rates in the United States overall are alarmingly high and on the rise, they are even higher amongst physicians and those training to be physicians, including medical students, residents, and fellows. One study found that a physician's risk of suicide is 130% higher than the general population for a female physician and 70% higher for a male.⁵³

Medical school is the first step in a long, stressful for someone training to become a doctor. For this reason, it is important to understand and address the mental health problems of medical students in order to develop a healthy workforce of future physicians. Published estimates of suicidal ideation among medical students worldwide vary by study ranging from 4.9% to 35.6%.⁵⁵ The purpose of this systematic review is to examine the existing literature on suicidality among United States medical students in order to better understand the scope of the problem so that appropriate interventions can be designed and implemented.

Key Question

This review focuses on the prevalence of suicidality, which encompasses suicidal ideation, suicidal behaviors, and suicide attempts, among medical students at U.S. allopathic medical schools. Many existing studies include international medical students, however because the sequence of training for U.S. medical graduates is unique, this review will look at these students alone.

Methods

Data Sources and Search Strategy

I searched PubMed, PsychInfo, and Embase for studies on US medical student mental health and wellbeing published in English between January 1, 2012 and June 2018. The searches included terms related to the population and setting of interest (medical students and medical school), as well as the outcomes of interest for the body of the paper above, including depression, anxiety, and suicidality. In PubMed, Medical Subject Headings (MeSH terms) were used as search terms when available. The full search strategy for these databases is detailed in Appendix B. ClinicalTrials.gov was also searched for unpublished literature on the topic, and Prospero was searched for ongoing systematic reviews, but neither returned relevant results. In addition, although this search excluded other systematic reviews, the bibliographies of relevant systematic reviews were examined to complete the article search process.

Study Selection

Titles, abstracts, and full-text articles were reviewed to determine eligibility using pre-defined inclusion and exclusion criteria. Full inclusion and exclusion criteria for this entire paper are presented in Table 1 in Appendix A of the paper above. Of the eligible articles, only those that measured suicidality were included for this specific systematic review. In short, the included studies measured suicidal ideation or self-reported suicide attempts among medical student at U.S. allopathic medical schools between 2012 and 2018. The year 2012 was chosen as the cut-off date because it marks the year that a pass-fail grading system for pre-clinical curriculums was formally endorsed by the AMA. To this date, the adoption of a pass-fail grading system has been one of

the only interventions that has consistently proven to improve the mental health of medical students.¹⁰

Data Extraction and Quality Assessment

Excel was used for data extraction and quality assessment of the relevant articles. Information such as study design, location, sample size, response rate, screening tool used, and results, as well other basic characteristics about each study were extracted and are presented in Table C1 below. For quality assessment, the Appraisal tool for Cross-Sectional Studies (AXIS tool) was used.⁵⁶ The quality assessment of each study can be found in Table C2.

Data Synthesis and Analysis

Due to the heterogeneity of studies and the outcome measurement tools used, an advanced quantitative meta-analysis of the data was not possible. Instead, the results section of this review includes a description of my findings and a critical analysis of the body of literature that exists on this topic.

Results

Search Results

The search strategy described above returned a total of 8 relevant studies. However, data extraction and clinical appraisal were only completed for 5 of the studies because several studies used the same original dataset. When multiple articles reported on the exact same data, I used my judgment to include only the study or studies most relevant to this particular review. Specifically, the article by Jackson, et.al.⁴⁹ was not included because it presented the same exact data as the article by Dyrbye, et.al.⁴⁷, but focused more on the outcomes of burnout and substance use,

rather than suicidality. The articles by Martinez, et.al.⁵⁰ and Moutier, et.al.⁵² were also not included because they used the same data set from the HEAR program at UC-San Diego as the articles by Downs, et.al.⁴⁶ and Zisook, et.al.⁵³, but did not report on suicidality of medical students alone. Instead, these articles included aggregated data that combined findings for medical students along with findings for residents, and faculty. A PRISMA diagram presenting the results of the search process is presented in Figure C1.

Study Characteristics

All of the included studies were cross sectional in design and based on the results of surveys that were completed by voluntary participants. Response rates ranged from 16.4%-34%. All 8 articles included medical students from all 4 years of study, and the 7 that reported respondent demographics all included a disproportionately high female sample.^{46-47,49,50-53} Five studies took place at a single institution (1 at Wayne State University⁴⁸ and 4 at UC-San Diego^{46,50,52-53}), while 2 were nationwide.^{47,49} One study, by Merlo, et.al.⁵¹ looked at all medical students in the state of Florida. Complete study characteristics can be found in Table C1.

Strength of Evidence

Several factors common to all of the included studies weaken the strength of evidence of this body of literature, as it exists right now. First, although a cross sectional design is appropriate for assessing prevalence, it cannot determine a causal relationship, so one cannot draw the conclusion that medical school, or any aspect of medical school, “causes” suicidality among students. Secondly, all studies measure suicidality using surveys, which are self-reported and completely voluntary. This poses

a significant risk of selection bias, as those that decide to participate in the study might not be representative of the whole population from which they were recruited.

Furthermore, since this is a sensitive subject and participation was not mandatory, response rates were generally low which raises the risk of selection bias. Lastly, measurement bias is a concern because several of the studies either did not include their exact measurement tool, or did not cite the sources that validated the tools they chose to use. Full clinical appraisal of each of the included studies using the AXIS tool is included in Table C2.

Prevalence of Suicidality

The prevalence of suicidality reported by the included studies ranged from 7.8% (N=27 in a sample of 343 students)⁴⁶, to 11.8% (N=102 in a sample of 862 completed surveys).⁵¹ The nationwide studies by Dyrbye, et.al. and Jackson, et.al., which included the largest and most geographically representative sample of students reported prevalence of suicidal ideation at 9.4% (N=414 in a sample of 4,402 students).^{47,49}

Notably, one study asked students both about suicidal ideation in the past year, as well as suicidal ideation at any point in their lives. The rate of lifetime suicidal ideation in that sample was 29.9% (N=115/385).⁴⁸

Heterogeneity of Screening Instruments

As discussed above, a meta-analysis of the study results is not possible due to the high level of heterogeneity between the articles. In the sample of included studies, a total of 4 different screening tools were used, ranging from one-item assessments^{47, 49,51} to a more thorough 5-item questionnaire used by the HEAR program.^{46, 50,52,53} Two of the studies that used the HEAR data did not disaggregate

medical student data from the data of house staff and faculty, so the data was not extractable.^{52, 53} This leaves a pool of 6 studies using 4 different outcome measures.

Discussion

This systematic review included a total of 8 studies (5 for data extraction and quality assessment), and 6,018 U.S. medical students. It focused on the prevalence of suicidality among this population, a group known to have higher rates of suicide and suicidal ideation than the general population outside of the medical field. The prevalence of suicidality measured by the studies included in this review ranged from 7.9%-11.8%, which is significant because it means that about 1 in every 10 medical students surveyed has had thoughts of ending their own life while in medical school.

Limitations

A systematic review on this topic has several limitations. First, this review was limited by a general paucity of literature overall. Of the 39 studies identified for the paper above that addressed anxiety, depression, and suicidality among U.S. medical students, only 8 included data on suicide. Thus from the beginning, this review was limited to a very small group of studies. Secondly, the quality of the review is severely limited by the heterogeneity of the data. Among the 5 studies from which data was extracted, there were 4 different outcome measures with varying levels of validity and reliability, making it difficult to do a high quality meta-analysis of the results.

Another major limitation of this body of literature comes from study design. All of the relevant articles were cross sectional studies that used self-reported survey tools for measurement. Because participation was completely voluntary, the results are limited by selection bias as there is no way to ensure that the sample that ultimately chose to

participate in the study is representative of the entire population. The risk of selection bias was increased by the overall poor response rate, which averaged only about 25%.

Measurement bias is also a concern, as there is no consensus on a single, validated screening tool for suicidality. The majority of the studies included used tools that they had tailored to meet their particular research needs. Furthermore, the surveys asked about sensitive topics, so as with all self-reported outcomes, it is possible that students were not completely honest with their answers. Poor response rates, heterogeneous screening tools, and a legitimate risk of untruthful answers severely limit both the internal and external validity of the studies' findings.

Future Directions for Research

There are several ways that future research can improve and build on this existing body of literature. For one, the cross sectional design of the studies included in this review could be improved by following students over time. With a more longitudinal design, schools could track the mental health of their students throughout their medical school journey, and hopefully identify appropriate points where intervention is necessary. Secondly, researchers should work to develop a single, validated tool for screening for suicide risk in this population. The tool should be a thorough risk assessment that can be adopted by schools throughout the country.

Most importantly, given that we know that medical students are at high risk for depression, anxiety, burnout, and other mental illnesses, it is imperative that the medical education community ask about suicidal ideation frequently, and using well-validated tools. Not only will this improve the quality and quantity of available data, but also it will allow us to truly understand the scope of the problem and design appropriate

interventions. Healthy communities need healthy providers, and healthy providers start their training in medical school. Thus, it should be a public health priority to appropriately evaluate and address the mental health needs of medical students nationwide.

Funding

There was no funding for this review.

Figure C1: PRISMA Diagram

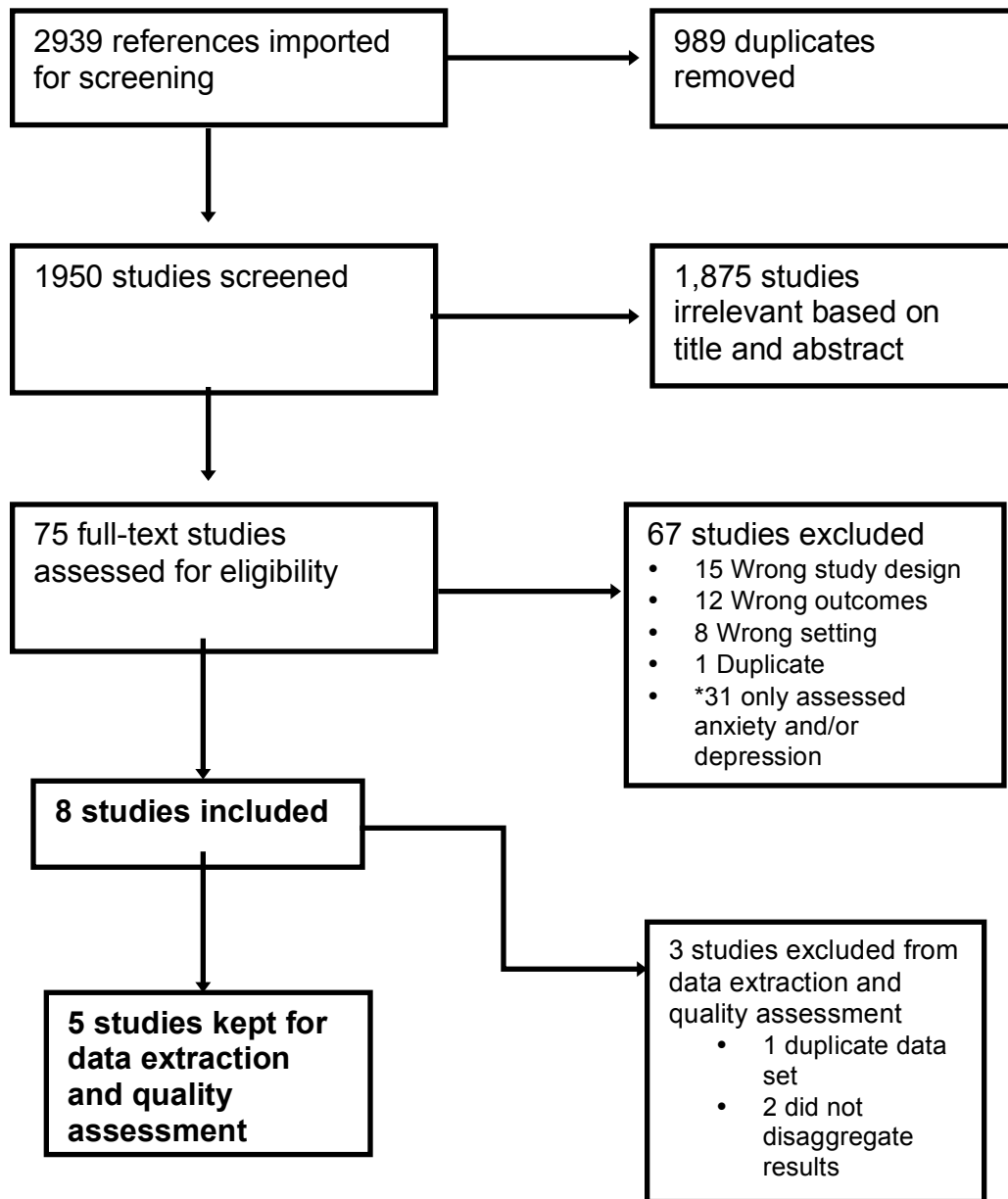


Table C1: Study Characteristics

First Author, - Year	Study Design	Location	Duration	Recruitment/ Concealment	N	Response Rate	Demographics		Suicide Screening Tool	Results	
							Age	Ratio of M:F		Suicidality	Past Suicide Attempt
MacLean (2016) ⁴⁸	Cross Section	Wayne State	1 yr.	Email invitation. Voluntary participation with possibility of monetary incentive. Fully anonymous	385	33% (385/1169)	Did not report	Did not report	3 Items from the Meehan Suicide Inventory	N=14 (11.7%) in past year. N=115 (29.9%) lifetime	N=7 (1.8%)
Merlo (2017) ⁵¹	Cross Section	All 9 medical schools in the state of Florida	1 yr (2014)	Emails, announcements, and flyers containing online link. Fully anonymous	862	17% (862/5053)	Did not report	42.9%M 57.1% F	One item screen	N=102 (~11.8% of completed surveys)	Did not ask
	Cross Section			Emailed medical students listed in AMA's PMF who had							

Jackson (2016) ⁴⁹	Exact same data as Dyrbye, but not as applicable as its focus is on burnout and substance use, versus suicidality.										
Downs (2014) ⁴⁶	Cross Section Time Series	UC-San Diego Medical School	4 yrs (2009- 2013)	Email invitation, voluntary participation, voluntary disclosure of identity.	343	34% (343/1008)	Y1:24.7, Y2:25.7, Y3:25.7, Y4:26.3	40.2%M 59.2%F	5 item risk assessment	N =27 (7.8%)	N=6 (1.7%)
Zisook, (2016) ⁵³	Cross Section Time Series	UC-San Diego Medical School	5 yrs (2009- 2014)	Email invitation, voluntary participation, voluntary disclosure of identity.	369	33% (369/1134)	Mean= 25.46 (SD: 2.99)	43.6%M 56.4%F	5 item risk assessment	N=38 (10.3%)	N= 6 (1.6%)
Martinez (2016) ⁵⁰	Same data set as Zisook and Downs, but suicidality in medical students alone is not reported separately from house staff and faculty.										
Moutier (2012) ⁵²	Same data set as Zisook and Downs, but suicidality in medical students alone is not reported separately from house staff and faculty.										

Table C2: Quality Assessment of Articles using the AXIS Tool⁵⁷

First Author, Year		MacLean (2016) ⁴⁸	Merlo (2017) ⁵¹	Dyrbye (2014) ⁴⁷	Downs(2014) ⁴⁶	Zisook (2016) ⁵³
Introduction	Were the aims/objectives of the study clear?	Yes: understand rates of depression, anxiety, suicidal behavior, and drug use in medical students	Yes: obtain a multi-institutional assessment of substance use, psychological distress, and help seeking among medical students in Florida	Yes: compare prevalence of burnout and other forms of distress across career stages, and versus those of the general population of college graduates	Yes: describe a 4 year trial of the HEAR program at UCSD	Yes: present data on the HEAL program's progress over its first 5 years of implementation
	Was the study design appropriate for the stated aim(s)?	Yes- cross sectional is appropriate for prevalence studies.	Yes- cross sectional is appropriate for prevalence studies.	Yes- cross sectional is appropriate for prevalence studies.	Yes- cross sectional is appropriate for prevalence studies.	Yes- cross sectional is appropriate for prevalence studies.
Methods	Was the sample size justified?	Yes	Yes	Yes	Yes	Yes
	Was the target/reference population clearly defined? (Is it clear who the research was about?)	Yes	Somewhat. The stated goal of the study is to assess prevalence among students in one state (Florida) but the authors state in the methods that their goal was a representative sample of medical students. Do they mean just in Florida or among all students?	Yes	Yes	Yes

Was the sample frame taken from an appropriate population base so that it closely represented the target/reference population under investigation?	Yes: all medical students at Wayne State were invited to participate	Yes: medical student at all 9 FL medical schools were invited to participate	Unclear: medical students were recruited by email using the PMF database. Authors state that this database includes almost all US students, however they only emailed those that had given the AMA permission to contact them via email	Unclear: Authors state that 2,968 individuals were invited to participate, but that 343/1008 participated. What does the 1008 represent?	Yes: all medical students at UCSD were invited to participate
Was the selection process likely to select subjects/participants that were representative of the target/reference population under investigation?	No- self selecting via voluntary participation in the study	No- self selecting via voluntary participation in the study	No- self selecting via voluntary participation in the study	No- self selecting via voluntary participation in the study	No- self selecting via voluntary participation in the study
Were measures undertaken to address and categorize non-responders?	No	No	Yes: compared demographics of respondents to full population of US medical students	No	No
Were the risk factor and outcome variables measured appropriate to the aims of the study?	Yes	Yes	Yes	Yes	Yes

	Were the risk factor and outcome variables measured correctly using instruments/measures that had been trialed, piloted or published previously?	We don't know. The researches used a 47-item survey that included questions taken from validated tools. We don't know the exact questions asked, cannot say whether together, the tool was validated	We don't know. Research questionnaire was created specifically for this study based on expert suggestions. The 98-item tool was assessed for content validity by an expert panel and face validity by deans, other physicians, and a sample of medical students. No formal reliability analysis was conducted.	Yes. The full survey is not provided, but all measures as reported in the methods were validated tools	We don't know. The HEAR questionnaire items were "modified" from the AFSP's Depression Suicide Screening Project Survey, but we don't know how many changes were made. Its use of 5 questions was more extensive than other studies in the group	We don't know. The HEAR questionnaire items were "modified" from the AFSP's Depression Suicide Screening Project Survey, but we don't know how many changes were made. Its use of 5 questions was more extensive than other studies in the group
	Is it clear what was used to determine statistical significance and/or precision estimates? (e.g. p-values, confidence intervals)	No, only prevalence rates were reported	Not for all outcomes	Yes	Yes	Yes
	Were the methods (including statistical methods) sufficiently described to enable them to be repeated?	Yes	Yes	Yes	Yes	Yes
Results	Were the basic data adequately described?	No, only prevalence rates were reported. We do not know anything else about the population of students reported on in the study	Somewhat. More demographic information about the sample should have been provided (mean age, race/ethnicity, etc)	Yes	Yes	Yes

	Does the response rate raise concerns about non-response bias?	Yes. Response rate = 33%	Yes. Response rate = 17% for full survey. Authors report higher in the paper by including everyone who started the survey	Yes. Response rate = 16.4%. Authors report higher in the paper by including only students who opened the email (not who received it)	Yes. Response rate = 34% (343/1,008) as reported by authors, but they also state that 2,968 email invitations were sent. If this is the case, than the response rate is actually only 11.5%	Yes. Response rate = 33%
	If appropriate, was information about non-responders described?	No	No	Yes (demographic information)	No	No
	Were the results internally consistent?	Yes	Somewhat. Because not everyone completed the survey, there was some missing data. Authors do not explicitly explain how this was dealt with	Yes	Yes	Yes
	Were the results presented for all the analyses described in the methods?	Yes	Yes	Yes	Yes	Yes
Discussion	Were the authors' discussions and conclusions justified by the results?	Yes	Yes	Yes	Yes	Yes
	Were the limitations of the study discussed?	Yes	Yes	Yes	Yes	Yes

Other	Were there any funding sources or conflicts of interest that may affect the authors' interpretation of the results?	No	No	No	No	No
	Was ethical approval or consent of participants attained?	Yes	Yes	Yes	Yes	Yes